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NIH-SUPPORTED FINDING ON COCAINE ADDICTION: TINY MOLECULE, BIG PROMISE

Discovery could lead to better ways of predicting drug abuse risk and treating addictions

A specific and remarkably small fragment of RNA appears to protect rats against cocaine addiction—and may also protect humans, according to a recent study funded by the National Institute on Drug Abuse (NIDA), a component of the National Institutes of Health. The study was published today in the journal Nature.

RNA (ribonucleic acid) molecules are known to play critical roles in the translation of genetic information (DNA) into proteins, which are the building blocks of life. In the past decade, scientists have begun to notice, catalogue and characterize a population of small RNAs, called microRNAs, that represent a new class of regulatory molecules. In this study, researchers at The Scripps Research Institute in Jupiter, Florida found that cocaine consumption increased levels of a specific microRNA sequence in the brains of rats, named microRNA-212. As its levels increased, the rats exhibited a growing dislike for cocaine, ultimately controlling how much they consumed. By contrast, as levels of microRNA-212 decreased, the rats consumed more cocaine and became the rat equivalent of compulsive users.

The study's findings suggest that microRNA-212 plays a pivotal role in regulating cocaine intake in rats and perhaps in vulnerability to addiction. Interestingly, the same microRNA-212 identified in this study, is also expressed in the human's dorsal striatum, a brain region that has been linked to drug abuse and habit formation.

"This study enhances our understanding of how brain mechanisms, at their most fundamental levels, may contribute to cocaine addiction vulnerability or resistance to it," said NIDA Director Dr. Nora D. Volkow. "This research provides a wonderful example of how basic science discoveries are critical to the development of new medical treatments and targeted prevention."

Rats with a history of extended cocaine access can demonstrate behavior similar to that observed in humans who are dependent on the drug. Current data show that about 15 percent of people who use

cocaine become addicted to it. This study's findings suggest that microRNAs may be important factors contributing to this vulnerability.

"The results of this study offer promise for the development of a totally new class of anti-addiction medications," said Paul J. Kenny, senior author on the study and an associate professor at the Scripps research facility. "Because we are beginning to map out how this specific microRNA works, we may be able to develop new compounds to manipulate the levels of microRNA-212 therapeutically with exquisite specificity, opening the possibility of new treatments for drug addiction."

The study, Striatal MicroRNA Controls Cocaine Intake Through Regulation of CREB Signaling, was authored by Jonathan A. Hollander et al., and can be found online at http://www.nature.com/nature/journal/v466/n7303/full/nature09202.html. Additional information on cocaine can be found at http://drugabuse.gov/DrugPages/Cocaine.html and http://www.drugabuse.gov/scienceofaddiction/.

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